Table 15: **Nef**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(1–20)	Nef(1–20 LAI)	MGGKWSKSSVVGWPT-VRERM	Vaccine	murine(H-2^d)	[Hinkula1997]
Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev					
Nef(16–35)	Nef(16–35 LAI)	VRERMRRAEPAADGV-GAASR	Vaccine	murine(H-2^d)	[Hinkula1997]
Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev					
Nef(31–50)	Nef(31–50 LAI)	GAASRDLEKHGAITSS-NTAA	Vaccine	murine(H-2^d)	[Hinkula1997]
Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev					
Nef(45–69)	Nef(45–69 BRU)	SSNTAATNAACAWLE-AQEEEEVGFP	Vaccine	rat, chimpanzee( )	[Estaquier1992]
Vaccine: *Vector/type:* peptide prime with protein boost *Strain:* BRU *HIV component:* Nef • Antigenic domain: ATNAACAWL, priming with peptide enhanced subsequent Ab response to Nef protein immunization					
Nef(46–65)	Nef(46–65 LAI)	SNTAATNAACAWLEA-QEEEE	Vaccine	murine(H-2^d)	[Hinkula1997]
Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein • Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev					
Nef(61–80)	Nef(61–80 LAI)	QEEEEVGFPVTPQVPL-RPMT	Vaccine	murine(H-2^b)	[Hinkula1997]
Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev • Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein					

- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(66–97)	Nef(66–97 LAI)	VGFPVTPQVPLRPMT-YKAAVDLSHFLKEKGG-L	Vaccine	human( )	[Gahery-Segard2000a]

Vaccine: *Vector/type:* lipopeptide

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial
- A CD4+ T-cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 5/10 reacted to this Nef peptide
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual
- 5/12 tested had an IgG response to this peptide

Nef(76–95)	Nef(76–95 LAI)	LRPMTYKAAVDLSHF-LKEKG	Vaccine	murine(H-2^b)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(91–110)	Nef(91–110 LAI)	LKEKGGLEGLIHSQRR-QDIL	Vaccine	murine(H-2^b)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(98–112)	Nef(98–112 BRU)	EGLIHSQRRQDILDL	Vaccine	chimpanzee( )	[Estaquier1992]

Vaccine: *Vector/type:* peptide prime with protein boost *Strain:* BRU *HIV component:* Nef

- Peptide alone could stimulate chimpanzee T-cells in the absence of carrier protein – required carrier protein in rat

Nef(104–123)	Nef(106–125 HXB3)	QRRQDILDLWIYHTQ-GYFPD?	Vaccine	murine(H-2^b)	[Sandberg2000]

Vaccine: *Vector/type:* DNA *Strain:* HXB3 *HIV component:* Nef

- A strong T-helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes

Nef(106–125)	Nef(106–125 LAI)	RQDILDLWIYHTQGYF-PDWQ	Vaccine	murine(H-2^b)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(117–147)	Nef(117–147 LAI)	TQGYFPDWQNYTPGP-GVRYPLTFGWCYKLVP	Vaccine	human( )	[Gahery-Segard2000a]

Vaccine: *Vector/type:* lipopeptide

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial
- A CD4+ T-cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 1/10 reacted to this Nef peptide
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual
- 10/12 tested had an IgG response to this peptide

Nef(121–140)	Nef(121–140 LAI)	FPDWQNYTPGPGVRY-PLTFG	Vaccine	murine(H-2^b)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(136–155)	Nef(136–155 LAI)	PLTFGWCYKLVPVEPD-KVEE	Vaccine	murine(H-2^d)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(151–170)	Nef(151–170 LAI)	DKVEEANKGENTSLL-HPVSL	Vaccine	murine(H-2^d)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

Nef(164–183)	Nef(166–185 HXB3)	LLHPVSLHGMDDPER-EVLEW?	Vaccine	murine(H-2^b)	[Sandberg2000]

Vaccine: *Vector/type:* DNA *Strain:* HXB3 *HIV component:* Nef

- A strong T-helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes

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Nef(166–185)	Nef(166–185 LAI)	HPVSLHGMDDPEREV-LEWRF	Vaccine	murine(H-$2^{b,d}$)	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

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Nef(179–203)	Nef(181–205 HXB3)	EVLEWRFDSRLAFHH-VAREL?	Vaccine	murine(H-2^{b})	[Sandberg2000]

Vaccine: *Vector/type:* DNA *Strain:* HXB3 *HIV component:* Nef

- A strong T-helper proliferative response against a rec Nef protein was observed 2 weeks after immunization of HLA-A201 transgenic mice in a C57Bl/6 background – the response was weak by 4 weeks post immunization
- Mice were immunized with nef DNA under the control of a CMV promotor, coated on gold particles delivered to abdominal skin by a gene gun
- Primary responses were directed at peptides 106-125, 166-185, and 181-205, indicating a response to multiple epitopes

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Nef(181–205)	Nef(181–205 LAI)	LEWRFDSRLAFHHVA-RELHPEYFKN	Vaccine	murine(H-2^{d})	[Hinkula1997]

Vaccine: *Vector/type:* DNA *Strain:* LAI *HIV component:* Nef, Tat, Rev

- Stronger, broader responses were observed in animals vaccinated with DNA epidermally rather than with intramuscular protein
- Some proliferative response to vaccination was observed to peptides throughout Nef and Tat, less for Rev

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Nef(182–205)	Nef(182–205 LAI)	EWRFDSRLAFHHVAR-ELHPEYFKN	Vaccine	human( )	[Gahery-Segard2000a]

Vaccine: *Vector/type:* lipopeptide

- Anti-HIV lipopeptide vaccine consisting of six long peptides derived from Nef, Gag and Env HIV-1 proteins modified by a palmitoyl chain was administered in a phase I trial
- A CD4+ T-cell proliferative response to at least one of the six peptides was observed in 9/10 vaccinees – 4/10 reacted to this Nef peptide
- 9/12 tested mounted a CTL responses to at least one of the six peptides, each of the six peptides elicited a CTL response in at least one individual
- None of the 12 tested had an IgG response to this peptide

Nef(185–200)	Nef(183–198)	FDSRLAFHHVARELHP	HIV-1 infection	human( )	[Ranki1997]

- T-cell response to this epitope persisted after seroreversion

Nef( )	Nef( )	HIV-1 infection	human( )	[daSilva1998a]

- This study compares the level of variation in Nef CTL epitopes to helper and MAb epitopes from the same region
- CTL epitopes tend to be more conserved than either helper or MAb epitopes and there are stronger functional constraints in the regions where CTL epitopes cluster

Nef( )	Nef( )	Vaccine	human( )	[Calarota1999a]

Vaccine: *Vector/type:* DNA *HIV component:* Nef, Rev Tat

- Nine HIV-1+ subjects were given one of three DNA vaccinations for nef, rev or tat, and novel proliferative and CTL responses were generated
- The nef DNA immunization induced the highest and most consistent CTLp activity, IFN-γ production, and IL-6 and IgG responses
- Highly active antiretroviral treatment (HAART) did not induce new HIV-specific CTL responses but reduced viral load, while DNA vaccination induced new immune responses but did not reduce viral load – thus this is a potentially complementary and promising combination

Nef( )	Nef( )	HIV-1 infection, Vaccine	human( )	[Calarota2001]

Vaccine: *Vector/type:* DNA *HIV component:* Nef, Rev, Tat *Stimulatory Agents:* CpG motifs

- This review discusses the cellular immune response, and comments on CpG induction of Th1 cytokines and enhanced immune responses, and HIV-1 DNA vaccine boosting of CTL and Th proliferative responses in asymptomatic HIV+ individuals

Nef( )	Nef( )	HIV-1 infection	human( )	[Oxenius2000b]

- Patients who started therapy at acute HIV infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable

Nef( )	Nef( )	Vaccine	murine(H-2^d)	[Ayyavoo2000a]

Vaccine: *Vector/type:* DNA *HIV component:* Vif, Vpu, Nef

- Splenocytes from BALB/c mice immunized with pVVN-P DNA were incubated with Vif, Vpu or Nef antigens for 3 days and assayed for IL-4 and IFN-γ levels
- Antigen stimulation increased IFN-γ production in pVVN-P immunized mice, indicating a Th1 response
- IL-4 production was not significantly changed after antigen stimulation compared to control levels
- Cross-clade CTL activity was also observed: A, B clade, CRF01(AE) clade antigens could serve as targets for the B clade immunization stimulated CTL – an HIV-1 AC recombinant, however, did not stimulate a CTL response, but was expressed at lower levels on the target cell